

Dapsone Hypersensitivity Syndrome in a Patient with Cutaneous Lupus Erythematosus

Sir,

Dapsone is a useful drug for treatment of various dermatological indications. It is known to have many side effects, of which the most common are methaemoglobinaemia and haemolysis. However, an uncommon, but severe, adverse effect is sulphone or dapsone hypersensitivity syndrome, which occurred in the case described here.

CASE REPORT

A 75-year-old woman who had had cutaneous lupus erythematosus for 18 months was initially treated with hydroxychloroquine. This treatment was stopped after 4 weeks because of nausea. She was then treated successfully with oral corticosteroids for 3 months and the steroid therapy could be discontinued. Her skin lesions relapsed some 5 months later and she was given dapsone 100 mg/day. Within 10 days she developed a high fever. Enlarged cervical lymph nodes were found and there was also a suspicion of urinary tract infection so she was given amoxicillin. One week later she felt worse, with a continuing high fever (39°C) and a generalized, non-itching, papular rash. Amoxicillin and dapsone were discontinued and she was admitted to our clinic 3 days later.

On admission she still had a high fever (40.2°C), an exfoliative dermatitis and hepatomegaly. Her cervical lymph nodes were no longer enlarged. ESR and CRP were normal. The haemoglobin level was 75 g/l (127 g/l 1 month earlier). The WBC count was $14 \times 10^9/l$, with a differential cell count of $5.5 \times 10^9/l$ neutrophils, $6.1 \times 10^9/l$ lymphocytes, $<0.1 \times 10^9/l$ eosinophils and $2.4 \times 10^9/l$ monocytes. Some atypical lymphocytes were seen both in peripheral blood and in bone marrow. Platelets were normal. Haptoglobin and reticulocytes were low, BCoHb raised with 3.79% (reference level 0.4–0.7%) and plasma Hb 0.18 g/l (reference level <0.02 g/l), which indicated both haemolysis and suppression of the bone marrow. There was no pathological methaemoglobin level. Liver enzymes were pathological, with: ALP 23 μ kat/l (normal 0.8–4.6 μ kat/l); γ -GT 11 μ kat (normal <1.20 μ kat/l); GOT 3.9 μ kat/l (normal <0.7 μ kat/l); GPT 4.0 μ kat/l (normal <0.7 μ kat/l); LDH 23 μ kat/l (normal <8.0 μ kat/l). Serum creatinine and G6PD levels were within normal limits.

The most likely diagnosis was dapsone hypersensitivity syndrome. Treatment with prednisone, 60 mg daily, was started, and there was a prompt resolution of the fever and gradual improvement of the symptoms. She left hospital 17 days after commencing treatment with prednisone. The skin lesions and the hepatomegaly had then disappeared, the liver enzymes were almost normalized, the WBC count was normal and the haemoglobin level 93 g/l. The prednisone dose was gradually reduced. The patient is now quite well, without any skin lesions.

DISCUSSION

Dapsone hypersensitivity syndrome consisting of fever, malaise, general rash transforming into an exfoliative dermatitis, hepatitis, lymphadenopathy, haemolytic anaemia and atypical lymphocytosis was first described by Lowe in 1950 (1), and was subsequently termed so by Allday & Barnes (2). This drug reaction was first observed in patients with

lepromatous leprosy, and the incidence of the syndrome has increased in the leprosy population since the introduction of multidrug therapy during the last decades (3). However, this reaction has also been reported in a variety of dermatological conditions (4–7) including lupus erythematosus (8).

The syndrome usually occurs during the first 3–8 weeks after the start of therapy. It closely resembles infectious mononucleosis, although there is no serological evidence of EBV, CMV or toxoplasma infection. The pathogenesis of the dapsone syndrome is unclear. Steroid response, improvement after drug withdrawal and occurrence at a wide range of daily dosages from 50 to 300 mg (8) suggests that it is an idiosyncratic hypersensitivity reaction to the drug. It may be caused by metabolites of dapsone-forming haptens with the formation of anti-dapsone antibodies (9). Treatment strategies include withdrawal of the drug and institution of systemic steroids. A long course of steroids may be needed despite the discontinuation of dapsone, as dapsone persists for up to 35 days in organs via protein binding and enterohepatic circulation (5). As dapsone is used increasingly (8), physicians should be aware of its potentially fatal side effects, especially when a patient treated with dapsone develops a high fever for unknown reasons.

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